

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

K is an alcohol containing from 1 to about 10 carbon atoms and at least one hydroxyl group, or a mixture of such alcohols.

49. (New) The composition of claim 48 wherein A is selected from the group consisting of acrylic acid and methacrylic acid.

Remarks

Claims 1-37 are pending. Claims 1, 21-28, 34, and 37 have been amended. New claims 38-49 have been added. A copy of all of the pending claims as they are believed to have been amended is attached to this Amendment as an appendix.

Claims 1, 21, 22 and 37 were amended to correct grammatical errors. Claim 21 was amended to depend from claim 1. Claims 22-28 were amended to correct antecedent basis. Claim 34 was amended to depend from claim 33.

New claims 38-48 are directed to compositions containing at least one macromer and at least one monomer. The monomer comprises at least 30% of the weight of the composition. Support for these claims can be found in the specification at least at page 9, line 23 until page 10, line 1, Table 2, and Examples 4, 5, 7, 8-15, 18, 21-23, 25, and 26. New claim 39 depends from claim 38 and describes the composition as a fluid or paste. Support for this claim can be found in the specification at least at page 8, lines 13-15. New claim 40 defines the composition as containing water. Support for this claim can be found in the specification at least at page 10, lines 1-6. New claim 41 defines the macromer as polyethyleneglycol-trimethylene carbonate-diacrylate. Support for this claim can be found in the specification at least at page 24, lines 17-24. Claim 42 more clearly defines the types of monomers that can be used in the composition.

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

A single monomer or a mixture of monomers can be used. Support for this claim can be found in the specification at least at page 9, lines 17-22. Claims 43 and 44 define the composition based on weight percentages. Support for these claims can be found in the specification at least at page 22, lines 7-8, 11-14, and 20-21. Claim 45 depends from claim 41 and defines the monomer as diacetone acrylamide. Support for this claim can be found in the specification at least at page 24, lines 17-26. Claim 46 further defines the composition based on the properties of the polymer which results from the copolymerization of the macromer and monomer. Support for this claim is claim 1, as originally filed. Claims 47-49 further define the macromer in the composition. Support for these claims can be found in the specification at least at page 40, lines 15-17 and in claims 21-23, as originally filed.

Response to Restriction Requirement

In the Office Action mailed November 21, 2001, the claims were divided into four groups, Group I, claims 1-20, 33-36, drawn to a polymer; Group II, claim 37, drawn to a method of using a polymer, Group III, claims 21-27, drawn to a compound, AHK, and Group IV, claims 28-32, drawn to a compound, AHC.

In response, applicants elect new claims 38-49 and the claims of Group I, if combined with claims 38-49, with traverse.

M.P.E.P. § 806.04 (b) states that compounds which are related to each other as intermediate and final product "are not independent and in order to sustain a restriction requirement distinctness must be shown." (Id.) Thus, a restriction requirement between Groups I, III, and IV is improper.

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

Further, claims 21-27 (Group III) have been amended to depend from claim 1 (Group I). Claims 21-27, as amended, more specifically define a monomer which is a part of the material defined by claim 1. Therefore Group III claims do not even define an intermediate composition. Group I claims are directed at materials which are used in the processes defined by Group II claims. Claim 1 recites the structure and properties of the polymerized material. Group III claims are directed to the methods of using these materials to treat biological tissue or in an implant. Thus, the claims of Group III are directed to the process of using of the materials defined by the Group I claims.

The new claims define compositions which form the materials described by the Group I and III claims. The new claims define compositions which can be used in the method claims of Group II.

Election of Species

In response to the election of species requirement, Applicants elect the species of claim 38.

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AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

Favorable consideration of claims 1-49 is earnestly solicited.

Respectfully submitted,



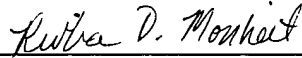
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Certificate of Mailing Under 37 C.F.R. § 1.8(a)

I hereby certify that this paper, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.



Rivka D. Monheit

Date: February 21, 2002

Marked Up Version of Amended Claims
Pursuant to 37 C.F.R. § 1.121(c)(1)(ii)

1. (Amended) A covalently [polymerized] polymerizable, water-absorbing, hydrogel-forming material,

wherein the material has both hydrophilic and hydrophobic regions and is polymerized to form a hydrogel characterized as having the following properties:
 - a) absorbing water to less than about 300% of its initial weight, on equilibration with water or bodily liquids;
 - b) having a solids content of at least about 20% after equilibration in water or bodily liquids;
 - c) having an elongation to failure of at least about 25% hydration to equilibrium; and
 - d) being sufficiently biocompatible to permit the treatment or repair of biological tissue, or used as an implant in a patient.
2. The material of claim 1, having a molecular weight after polymerization of at least 10 kDa.
3. The material of claim 1, which is covalently crosslinked.
4. The material of claim 1, which is non-covalently crosslinked.
5. The material of claim 1, having a tensile modulus of at least about 50 kPa after equilibrium hydration.
6. The material of claim 1, having an equilibrium water content of at least about 2%.
7. The material of claim 1, being capable of being formed *in situ* on body tissue or a medical implant by one or both of polymerization and crosslinking.

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

8. The material of claim 1, adhering to tissue when polymerized thereon.
9. The material of claim 1, being substantially elastic during a 10% elongation and release therefrom.
10. The material of claim 1, further characterized in being lubricious.
11. The material of claim 1, further characterized in comprising, before polymerization or crosslinking,
 - a) at least one component which is a macromer of molecular weight of about 1000 Da or more, at least 20% of the macromer being a hydrophilic block or region and comprising at least one chemically reactive group; and
 - b) at least one component bearing more than one chemically reactive group.
12. The material of claim 1, further characterized in comprising, before polymerization or crosslinking, at least 20% by weight of at least one amphiphilic water-soluble monomer of molecular weight less than about 1000 Da.
13. The material of claim 1, in which the water absorption at equilibrium hydration is less than about 200%.
14. The material of claim 1, in which the solids content is at least about 25% after equilibrium swelling.
15. The material of claim 1, in which the elongation to failure is at least about 200%.
16. The material of claim 1, in which the tensile modulus is at least 200 kPa.

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

17. The material of claim 1, further compromising a therapeutic, prophylactic or diagnostic agent.

18. The material of claim 1 formed by polymerization of a mixture comprising:

a) about 40% to about 100% by weight of one or more polymerizable monomers having a molecular weight of about 1000 Da or less;

wherein at least about 40% by weight of the monomers consists of amphiphilic monomers;

wherein no more than about 50% by weight of the monomers consists of functionally hydrophobic monomers;

b) 0% to about 40% by weight of a reactive macromer having a molecular weight greater than about 500 Da, which comprises on average more than one polymerizable group per molecule, and which has hydrophilic groups comprising about 20% of the macromer; and

c) 0% to about 40% water.

19. The material of claim 1 in the form of a coating on an implant or device.

20. The material of claim 1 forming an implant or device.

21. (Amended) [A] The material of claim 1, further characterized as comprising, before polymerization or crosslinking, a monomer having the formula AHK, wherein:

A is a residue of an ethylenically unsaturated acid that is linked to H by a bond selected from ester and amide;

H is the residue of a hydroxy carboxylic acid, a carbonic acid, or an amino acid, which is linked to K by an ester bond; and

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

K is the residue of an alcohol containing at least one carbon atom.

22. (Amended) The [monomer] material of claim 21 wherein

A is selected from the group consisting of acrylic, methacrylic crotonic, isocrotonic, tiglic, angelic, and cinnamic acids; maleic, fumaric, citraconic, mesaconic, itaconic, citric and isocitric acids, and monoesters and monoamides thereof, and mixtures thereof;

H is selected from the group consisting of glycolic acid, lactic acid, 3-hydroxy-propanoic acid, a hydroxybutyric acid, a hydroxypentanoic acid, hydroxy trimethylene carbonic acid, hydroxy ethylene carbonic acid, hydroxy propylene carbonic acid, hydrolyzed dioxanone [(i.e., 2-hydroxyethoxyacetic acid)], a hydroxyhexanoic acid, an alpha, beta or gamma amino acid of eight carbons or fewer, and mixtures thereof; and

K is an alcohol containing from 1 to about 10 carbon atoms and at least one hydroxyl group, or a mixture of such alcohols.

23. (Amended) The [monomer] material of claim 22 wherein A is selected from the group consisting of acrylic acid and methacrylic acid.

24. (Amended) The [monomer] material of claim 22 wherein H has one to about eight carbon atoms and is selected from the group consisting of glycolic acid, lactic acid, 3-hydroxy-propanoic acid, a hydroxybutyric acid, a hydroxypentanoic acid, and a hydroxyhexanoic acid.

25. (Amended) The [monomer] material of claim 22 wherein H is selected from the group consisting of hydroxy trimethylene carbonic acid, hydroxy ethylene carbonic acid, hydroxy propylene carbonic acid, and hydrolyzed dioxanone (i.e., 2-hydroxyethoxyacetic acid).

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

26. (Amended) The [monomer] material of claim 22 wherein H has two to eight carbon atoms and is selected from the group consisting of an alpha amino acid, a beta amino acid, a gamma amino acid, and mixtures thereof.

27. (Amended) The [monomer] material of claim 22 wherein K is selected from the group consisting of methanol, ethanol, propanol, isopropanol, isomers of butanol, isomers of pentanol, and isomers of hexanol.

28. (Amended) An intermediate [for the preparation of the monomer of claim 21 the intermediate] having the [form] formula AHC wherein A is a residue of an ethylenically unsaturated acid that is linked to H by a bond selected from ester and amide;

H is the residue of a hydroxy carboxylic acid, a carbonic acid, or an amino acid, which is linked to C by an acyl bond; and

C is a leaving group, which is displaced by alcohols to form esters.

29. The intermediate of claim 28, wherein the leaving group C is selected from the group consisting of halogens, succinimidyl group, imidazoles, thiols, nitrophenols, pyridines, and o-acyl ureas.

30. The intermediate of claim 28 wherein A is selected from the group consisting of acrylic, methacrylic crotonic, isocrotonic, tiglic, angelic, and cinnamic acids; maleic, fumaric, citraconic, mesaconic, itaconic, citric and isocitric acids, and monoesters and monoamides thereof; and mixtures thereof.

31. The intermediate of claim 28 wherein A is selected from the group consisting of acrylic acid and methacrylic acid.

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

32. The intermediate of claim 28 wherein H is selected from the group consisting of glycolic acid, lactic acid, 3-hydroxy-propanoic acid, a hydroxybutyric acid, a hydroxypentanoic acid, hydroxy trimethylene carbonic acid, hydroxy ethylene carbonic acid, hydroxy propylene carbonic acid, hydrolyzed dioxanone (2-hydroxyethoxy acetic acid), a hydroxyhexanoic acid, an alpha, beta or gamma amino acid of eight carbons or fewer, and mixtures thereof.

33. The material of claim 1, wherein the tissue is orthopedic tissue.

34. (Amended) The material of claim [1] 33, wherein the tissue is selected from the group consisting of bone, cartilage, meniscus, bursa, synovial membranes, tendons, ligaments, muscle and vertebral disks.

35. The material of claim 1, wherein the material is effective to provide lubricity, abrasion-resistance, load distribution, or resurfacing to an orthopedic tissue.

36. The material of claim 1, wherein the material adheres to tissue.

37. (Amended) A method for the treatment of biological tissue or a medical implant comprising [the application of]

applying a crosslinked polymeric hydrogel material to the tissue or implant, wherein the material has both hydrophilic and hydrophobic regions and is characterized as having the following properties:

- a) absorbing water to less than about 300% of its initial weight, on exposure to water or bodily liquids;
- b) having a solids content of at least about 20% after equilibration in water or bodily fluids;

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

c) having an elongation to failure of at least about 25% both as formed and after swelling to equilibrium; and

d) being biocompatible;

wherein the material is formed by the crosslinking of reactive monomers and macromers in the presence of tissue, and undergoes hydration with bodily liquids to form a water-containing material.

Please add the following new claims.

38. (New) A composition for forming a water-absorbing, high modulus polymeric material comprising at least one macromer and at least one monomer,

wherein the macromer comprises hydrophobic and hydrophilic regions and has a molecular weight of 500 to 200,000 Da,

wherein the monomer contains at least one vinyl group and has a molecular weight of less than 1,000 Da, and

wherein the monomer comprises at least 30% (wt/wt) of the composition.

39. (New) The composition of claim 38, wherein the composition is in the form of a fluid or paste.

40. (New) The composition of claim 38, further comprising water.

41. (New) The composition of claim 38, wherein the macromer is polyethyleneglycol-trimethylene carbonate-diacylate.

42. (New) The composition of claim 38, wherein the monomer is selected from the group consisting of vinyl caprolactam, methyl acrylate, methyl methacrylate, styrene, N-vinyl

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

pyrrolidone, and N-vinyl imidazole, diacetone acrylamide, vinyloxyethanol, 2-acrylamido-2-methylpropane, and methyl acryloyl lactate and mixtures and derivatives thereof.

43. (New) The composition of claim 38, wherein the macromer comprises up to 50% (wt/wt) of the formulation and the monomer comprises at least 45% (wt/wt) of the formulation.

44. (New) The composition of claim 43, further comprising less than 40% (wt/wt) water.

45. (New) The composition of claim 41, wherein the monomer is diacetone acrylamide.

46. (New) The composition of claim 38,
wherein upon copolymerization of the macromer and monomer, a polymeric material is formed, wherein the material comprises hydrophobic and hydrophilic regions and is characterized as having the following properties:

- a) absorbing water to less than about 300% of its initial weight, on equilibration with water or bodily liquids;
- b) having a solids content of at least about 20% after equilibration in water or bodily liquids;
- c) having an elongation to failure of at least about 25% hydration to equilibrium; and
- d) being sufficiently biocompatible to permit the treatment or repair of biological tissue, or used as an implant in a patient.

47. (New) The composition of claim 38, wherein the macromer has the formula AHK, wherein:

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

A is a residue of an ethylenically unsaturated acid that is linked to H by a bond selected from ester and amide;

H is the residue of a hydroxy carboxylic acid, a carbonic acid, or an amino acid, which is linked to K by an ester bond; and

K is the residue of an alcohol containing at least one carbon atom.

48. (New) The composition of claim 47 wherein

A is selected from the group consisting of acrylic, methacrylic crotonic, isocrotonic, tiglic, angelic, and cinnamic acids; maleic, fumaric, citraconic, mesaconic, itaconic, citric and isocitric acids, and monoesters and monoamides thereof, and mixtures thereof;

H is selected from the group consisting of glycolic acid, lactic acid, 3-hydroxy-propanoic acid, a hydroxybutyric acid, a hydroxypentanoic acid, hydroxy trimethylene carbonic acid, hydroxy ethylene carbonic acid, hydroxy propylene carbonic acid, hydrolyzed dioxanone, a hydroxyhexanoic acid, an alpha, beta or gamma amino acid of eight carbons or fewer, and mixtures thereof; and

K is an alcohol containing from 1 to about 10 carbon atoms and at least one hydroxyl group, or a mixture of such alcohols.

49. (New) The composition of claim 48 wherein A is selected from the group consisting of acrylic acid and methacrylic acid.